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CASE REPORT

Neuromyelitis optica with CSF examination mimicking bacterial meningomyelitis

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Abstract Neuromyelitis optica (NMO) is a rare inflammatory demyelinating disease of the central nervous system that causes severe attacks of optic neuritis and myelitis. Abnormal CSF findings are one of the characteristics of NMO that help to distinguish it from classical multiple sclerosis. Here we describe two cases of Devic's syndrome with CSF findings suggestive of bacterial meningomyelitis.

Keywords Neuromyelitis optica · Optic neuritis · Meningomyelitis

Introduction

Neuromyelitis optica (NMO) or Devic's syndrome is a rare inflammatory disorder consisting of one or more episodes of optic neuritis (ON) in combination with acute transverse myelitis (ATM). In contrast to typical multiple sclerosis (MS), these clinical events in NMO are usually more acute or even fulminant and severe [1]. Devic's syndrome may follow either a monophasic or relapsing course with several important differences regarding the onset, severity and long-term prognosis of disease [2]. The diagnosis of neuromyelitis optica, despite well-defined criteria and the possibility of serological confirmation (NMO-IgG), could be very challenging, particularly in cases with a long time interval between the optic neuritis and the myelitis attack [3, 4]. In addition, NMO has been associated with numerous systemic autoimmune and infectious diseases [5].

One of the characteristics that distinguishes it from classical MS is the cerebrospinal fluid (CSF) finding. In patients with NMO, CSF examination during an active phase of the disease often reveals at least one abnormality (up to 65.9%) [6]. The most common is pleocytosis that can be dominated by polymorphonuclear cells followed by an increased total protein concentration level [7, 8].

The authors present two cases of NMO with CSF findings mimicking bacterial meningomyelitis.

Case 1

A 47-year-old white female was admitted to the neurology ward of another hospital in October 2007 because of sudden and severe pain in the neck, back and lumbar region spreading to the groins and both legs. During the next 2 days she reported weakness, which evolved into flaccid paraplegia accompanied with complete sensory loss caudal to her breast and loss of bladder and bowel control. In addition, decreased visual accuracy in the central visual field of her left eye and fever was noted. CSF examination revealed neutrophilic pleocytosis with increased total protein concentration and the patient was transferred to our hospital for suspected bacterial meningomyelitis.

The careful medical history taking revealed the patient was blind in her right eye because of optic neuritis twenty years ago. Five weeks prior to the actual disease she was

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admitted to the ophthalmologic ward because of painless decreased visual acuity in her left eye following a common cold. She was treated with low dose steroids for fifteen days and discharged from hospital with minimal visual improvement.

There was no history of sexually transmitted diseases, arthritis, arthralgias, rash, exposure to tuberculosis or other illnesses in the recent months.

Her body temperature was 37.6°, pulse 96 and respirations 20. Blood pressure was 135/51 mmHg. She complained of terrible pain in her neck. Physical examination was otherwise unremarkable. On neurologic examination, the patient was alert and oriented. She reported blindness in her right eye and severe decreased visual acuity in the left eye (20/100). Meningeal signs were positive. Deep tendon reflexes on the lower extremities and plantar responses were absent. Flaccid weakness in both legs and complete sensory loss caudal to her breast were noted.

Erythrocyte sedimentation rate was 128/h, C-reactive protein 97.4 mg/l, fibrinogen 7.44 g/l. Complete blood count and urine were normal. The patient's immunoglobulin profile was normal. Procalcitonine was <0.5 ng/ml. CD4+ lymphocyte count was decreased (80 per mm^3). A lumbar puncture revealed opalescent CSF that contained 540 cells/mm^3 (neutrophils 73%), the total protein level was 1,033 g/l and glucose level was 1.6 mmol/l (CSF-blood glucose ratio was 0.301). Blood–brain barrier was damaged. CSF concentration of neuron-specific enolase (NSE) was 76 μg/l (normal range 0–15.5 μg/l), protein Tau 1,450 pg/ml (normal range 80–149.8 pg/ml) and S-100 62 μg/l (normal range 0–2.5 μg/l). Protein 14-3-3 was also positive in the CSF.

Spinal MRI demonstrated increased signal on T2-weighted image in cord segments C7 to Th5. The affected region showed minimal enhancement with gadolinium. Chest radiography, brain CT scan and brain MRI showed no abnormalities. An electroencephalogram taken on admission showed normal 9 Hz alpha rhythm. All culture samples taken at admission were sterile and negative, respectively (blood, CSF and urine). EBV DNA, CMV DNA and HSV DNA were not detected in the CSF and blood samples. Stool samples for isolation of polio I, II and III viruses, echoviruses, and coxsackieviruses were negative. Tests for antibodies (blood and CSF samples) against herpes simplex virus 1 and 2, varicella-zoster virus, human herpes virus type 6, Epstein–Barr virus, cytomegalovirus, tick-borne encephalitis virus, *Mycoplasma pneumoniae*, *Chlamydia pneumoniae*, *Borrelia burgdorferi*, and Brucella were negative. Test for human immunodeficiency virus 1 and 2 antibodies was negative. Treponema pallidum haemagglutination test (TPHA) was negative. CSF culture samples for *Mycobacterium tuberculosis* and fungi were also negative.

Rheumatoid factor, antinuclear factor, cytoplasmic anti-neutrophil antibodies and anticardiolipin antibodies were also negative. Total serum complement, C3 and C4 component of the complement as well as angiotensin-converting enzyme levels were normal.

The patient was treated with 500 mg methylprednisolone IV for the first 8 days with subsequent dose tapering during the next 3 weeks. Besides steroids, the patient also received ceftriaxone for the first 5 days. Applied therapy resulted in visual acuity improvement in her left eye (20/50) and partial recovery of the flaccid paraplegia, but with persistent paresthesias. The pain completely disappeared. However, bowel and bladder control was not established. CSF findings during the patient's stay in the hospital are shown in Table 1. Since the infective causes of myelitis were excluded, the patient was transferred back to the neurology ward. The expanded disability status scale (EDSS) score was 8.5. The patient was discharged from hospital and the outpatient treatment was continued with 16 mg methylprednisolone per day.

Five months later, the patient was admitted again to our ward because of subacute onset of severe relapse of myelitis. CSF examination revealed only mild elevation of the total protein level, but the spine MRI showed extensive cervical and thoracic spinal cord involvement. Plasmapheresis was performed (five exchanges every other day, 50 ml/kg each) with excellent response. The long-term treatment was continued with 100 mg azathioprine and 12 mg methylprednisolone per day. The EDSS score at discharge was 8.5.

Case 2

A 60-year-old white male was admitted to the neurology ward of another hospital in February 2008 because of sudden pain in the abdomen and loins, followed by weakness in his legs and bladder dysfunction. The next day the weakness progressed to flaccid paraplegia with paresthesias in the legs and genital area, accompanied with decreased acuity of vision in his right eye. The patient also reported hypesthesia caudal to his pelvis. CSF examination revealed neutrophilic pleocytosis with increased total protein level and hypoglycorrhachia. The patient was immediately transferred to our hospital for suspected bacterial myelitis.

The careful medical history taking revealed that the patient had been almost blind in his left eye for more than 20 years. He could not recall what exactly happened with his eye and he attributed the vision loss to asbestos fibers exposure at his work. He did not seek medical attention until a few years ago when amblyopia was diagnosed. He was a carpenter with no history of illnesses in the recent

Table 1 CSF findings in patients during steroid treatment

CSF	Days of steroid treatment								Normal range
	1	2	3	4	5	10	19	25	
Cells/mm^3 (neutrophils %)									
Pt 1	540 (73)	566 (72)	93 (43)	26 (33)	–	15 (1)	–	9 (0)	3–5
Pt 2	4,864 (61)	1,605 (82)	–	–	13 (3)	–	3 (0)		cells/mm^3
Protein									
Pt 1	1.033	1.255	0.835	0.658	–	0.332		0.574	0.15–0.45 g/l
Pt 2	3.090	2.833	–	–	0.588	–	0.389	–	
Glucose									
Pt 1	1.6	1.9	3.5	3.2	–	3.5	–	3.9	2.25–4.0 mmol/l
Pt 2	1.7	2.2	–	–	4.5	–	6.0	–	
Chloride									
Pt 1	121	124	130	132	–	127	–	122	118–132 mmol/l
Pt 2	122	121	–	–	128	–	121	–	
CSF–blood glucose ratio									
Pt 1	0.301	0.240	0.388	0.438	–	0.5	–	0.709	>0.4
Pt 2	0.261	0.379	–	–	0.529	–	0.821	–	

Pt 1 patient 1, *Pt 2* patient 2

months. He took no drugs and denied any history of tick bites, arthritis, arthralgias, sexually transmitted diseases, rash or exposure to tuberculosis.

His body temperature was 36.1°C, pulse 60 and respirations 18. Blood pressure was 155/80 mmHg. Glasgow coma scale score was 15. Meningismus was present. Physical examination was normal. On neurologic examination, the patient reported bilateral decreased visual acuity, 20/400 (6/120) in the left eye and 20/100 (6/30) in the right eye. The sensation diminished below his pelvis. Flaccid weakness in both legs with absent deep tendon reflexes was noted. Plantar responses were absent and loss of bladder control was present.

Erythrocyte sedimentation rate was 20/h, C-reactive protein 10.5 mg/l and fibrinogen 3.7 g/l. Complete blood count and immunoglobulin profile were normal. CSF findings are shown in Table 1. Blood–brain barrier was damaged. Oligoclonal banding in CSF was negative.

Chest radiography and brain CT scan revealed no abnormalities. Brain MRI showed only small amount of effusion in the left optic nerve sheath. Spinal MRI revealed longitudinal lesion that included lower cervical and thoracic spinal cord swelling and increased intramedullary T2 signal. Gadolinium enhancement of the entire affected spinal cord was detected.

All culture samples were negative (blood, CSF and urine). EBV DNA, CMV DNA and HSV DNA were not detected in the CSF and blood samples. PCR-based assays for *Streptococcus pneumoniae* and *Staphylococcus aureus* from CSF samples were negative.

Test for human immunodeficiency virus 1 and 2 antibodies was negative. Treponema pallidum hemagglutination test was negative. CSF culture samples for *Mycobacterium tuberculosis* were also negative. Angiotensin-converting enzyme level was normal. Treatment with dexamethasone (48 mg per day for the first 7 days) was initiated at admission, accompanied by cloxacillin and ceftriaxone for the first 4 days. After the first week, the patient was treated with tapering doses of methylprednisolone for the next 3 weeks with partial recovery of paraplegia and improvement of visual acuity in the right eye. However, paresthesia did not abate and bladder dysfunction persisted. The patient was transferred back to the neurology ward. At discharge from our hospital, he was taking 24 mg methylpredisolone per day. During his stay at the neurology ward, total plasma exchange (TPE) was performed (seven times, every other day) but without any benefit. He was discharged from the hospital with an EDSS score of 8.0 and the outpatient treatment was continued with methylprednisolone 12 mg per day.

After 6 months, the patient was admitted again because of a sudden onset of weakness and paresthesias in both arms. MRI showed extensive cervical spinal cord enlargement and increased intramedullary T2 signal with gadolinium enhancement. Thoracic spinal cord showed no new changes.

Because of a previous unsuccessful treatment with plasmapheresis, a high-dose steroid treatment (1 g methylprednisolone/day for 5 days) was attempted, but failed to achieve any improvement. The patient was discharged from the hospital with an EDSS score of 9.0.

Discussion

We report two patients with Devic's syndrome and unusual CSF findings. Both of them met two major and two minor diagnostic criteria for NMO [3]. Furthermore, both patients developed relapses of the disease several months after the first attack, which additionally supported clinical diagnosis. Unfortunately, confirmatory NMO-IgG test could not be performed.

The onset of the disease and symptoms in both patients were suggestive of acute transverse myelitis. In addition, the signs of preceded optic neuritis were present in both of them. However, the surprising CSF findings with neutrophilic pleocytosis and hypoglycorrhachia demanded extensive diagnostic workup and initiation of antimicrobial treatment. Furthermore, an urgent MRI of the spine was also required to exclude spinal cord compression. Despite comprehensive diagnostic efforts, we did not find any concomitant systemic inflammatory or infective diseases in our patients.

The medical history of the patients, clinical presentation with relapsing course of the disease, MRI findings and fast conversion of the CSF findings into mononuclear low-grade pleocytosis confirmed our first clinical impression. Furthermore, there was a significant clinical improvement related to the initiation of steroid treatment. Neutrophilic pleocytosis with increased total protein level and absolute hypoglycorrhachia reflected the severity of myelitis. The first patient also had increased concentrations of Tau, S-100, NSE and 14-3-3 proteins in the CSF, indicating an acute and severe neuronal damage. Similar CSF findings with neutrophilic pleocytosis and increased protein level were already described during the acute phase of NMO [6–8]. However, as far as we know, this is the first report of an absolute hypoglycorrachia in patients with NMO.

In cases with CSF findings similar to ours, the diagnosis could be doubtful and frequently require comprehensive diagnostic workup to exclude other diseases, particularly in patients with meningomyelitis and uncertain history of optic neuritis. Because of that, the correct diagnosis and timely initiation of appropriate treatment could be missed. It should be stressed that established neurological damage due to myelitis and optic neuritis in untreated patients is permanent. Accordingly, it is of outstanding importance to commence adequate (immunosuppressive) treatment without any delay in such patients.

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Conflict of interest statement None.

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